September 9, 1998

This document was submitted to EPA by a registrant in connection with EPA's evaluation of this chemical and it is presented here exactly as submitted.

Pages (16-56) of Document #41 is Releasable to persons who submit a signed "Affirmation of Non-Multinational Status"

Please See Docket Staff for a Copy of the Affirmation.

8M 4E/OPP#34134

Bayer

Agriculture Division

January 8, 1998

Bayer Corporation
8400 Hawthorn Road
P.O. Box 4913
Kansas City, MO 64120-0013
Phone: 816 242-2000

Cynthia Giles-Parker
Product Team 22
Registration Division - H7505C
Office of Pesticide Programs
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460-0001

Subject: Import Tolerance Petition for Fenamiphos on Coffee and Cantaloupe
Pesticide Petition No. 9E3721

Dear Ms. Giles-Parker:

On December 2, 1997 we submitted an FQPA document for the subject petition per PR Notice 97-1. This FQPA document contained a Monte Carlo acute dietary analysis. Since that time, we received a letter, dated December 16, 1997, from Walter I. Waldrop of the Special Review and Reregistration Division. Enclosed with this letter was a September 18, 1997 memorandum from the Science Analysis Branch, Health Effects Division reporting on the conclusions of the Hazard Identification Assessment Review Committee's recent review of the toxicology database for fenamiphos. The committee concluded that the endpoint for acute dietary assessment should now be 0.37 mg/kg/day (LOEL from a rat acute neurotoxicity study). The previous acute endpoint was 0.5 mg/kg/day. In addition, the EPA has determined that an additional threefold uncertainty factor should be used for enhanced sensitivity to infants and children since a NOEL was not established in the rat acute neurotoxicity study. As a result, for acute dietary assessment, a margin of exposure (MOE) of 300 is now required to ensure protection of infants and children. The previous MOE required was 100.

In response to this letter, we are submitting a revised FQPA document, dated January 8, 1998. The Monte Carlo acute dietary analysis in this revised FQPA document shows that even with the acute endpoint now at 0.37 mg/kg/day and the additional threefold uncertainty factor, the MOE is above 300 at the 99.9th percentile for the U.S. population and for the most sensitive population subgroup (children, 1-6 years).

Section 408(d)(2)(A)(I) of the FFDCA requires that a pesticide petition must contain an informative summary of the petition and of the data, information, and arguments submitted or cited in support of the petition. PR Notice 97-1 states that the Agency will use the Executive Summary of the FQPA Supplemental Information Document to satisfy its obligation to publish a Notice of Filing in the *Federal Register* under FQPA. Bayer agrees that the Executive Summary of this FQPA Supplemental Information Document or any information it contains may be published as a part of the notice of filing for the petition and as part of a proposed or final regulation issued. An electronic copy of our FQPA Supplemental Information Document, including its Executive Summary, is contained on the enclosed computer diskette in WordPerfect 5.1 format (file FQPACOFF.DOC).

If you have any questions concerning this submission, please contact Mr. Melvin Tolliver of my staff at (816) 242-2150.

Sincerely,

BAYER CORPORATION
AGRICULTURE DIVISION

John S. Thornton
Director, Product Registrations
and Regulatory Affairs

MKT798:mr

Enclosure: "FQPA Supplemental Information Document, Cantaloupe and Coffee Petition (PP 9E3721), (Pursuant to PR Notice 97-1)," dated January 8, 1998 (hard and electronic copy)

cc: Judy Loranger
U.S. EPA/OPP
Special Review and Reregistration Division, H7508W

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January 8, 1998

FQPA Supplemental Information Document
Cantaloupe and Coffee Petition (PP 9E3721)
(Pursuant to PR Notice 97-1)

I. Executive Summary

A. Toxicological Profile

1. Acute Toxicity
   - Rat acute oral study with an LD50 of 2.7 mg/kg for males and 3.0 mg/kg for females
   - Rabbit acute dermal of LD50 of 225 mg/kg for males and 178.8 mg/kg for females
   - Rat acute inhalation of LC50 of > 0.1 mg/L
   - Primary eye irritation study in the rabbit which showed slight irritation
   - Primary dermal irritation study showed no skin irritation
   - Primary dermal sensitization study showed no sensitization
   - Acute delayed neurotoxicity study showed that fenamiphos is not neurotoxic
   - Acute oral neurotoxicity study showed no treatment-related changes in mean body weights, absolute and relative brain weights and the incidence of gross and neurohistopathological lesions. Clinical signs were observed including plasma and red blood cell inhibition. The LOEL is 0.37 mg/kg. The NOEL was not identified.

2. Genotoxicity
   - An Ames study was negative.
   - A dominant-lethal test in mice was negative.
   - An in vitro assay in Chinese hamster ovary cells was negative.

3. Reproductive and Developmental Toxicity
   - A three-generation reproduction study with no reproductive effects at 30 ppm (HDT).
   - A teratology study in rabbits with developmental and maternal NOELs at 0.5 mg/kg.
   - A teratology study in rats with a maternal NOEL of 0.85 mg/kg and a developmental NOEL of 3.0 mg/kg (HDT).

4. Subchronic Toxicity
   - A 90-day rat feeding study with a no-observed-effect level (NOEL) of 4 ppm for cholinesterase inhibition.
   - A 90-day dog-feeding study with a NOEL of 1 ppm for cholinesterase inhibition.
   - A 21-day dermal exposure study showing no effects on plasma, erythrocyte, or brain cholinesterase activity at 0.5 mg/kg.
   - A 21-day inhalation study with a cholinesterase NOEL of 0.25 μg/L and a LEL of 3.5 μg/L.

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- A neurotoxicity study in hens showed no neurotoxicity damage at 12.5 mg/kg (HDT).
- A subchronic neurotoxicity screen study showed no treatment-related changes in mean body weights or absolute and relative brain weights. The incidences of gross and neuropathological findings of treated animals were comparable to controls. Based on plasma and red blood cell inhibition the LOEL was established at 10 ppm and the NOEL at 1 ppm.

5. Chronic Toxicity
   - A 2-year rat feeding/carcinogenicity study with a NOEL for cholinesterase inhibition at less than 2.0 ppm (equivalent to 0.1 mg/kg/day) and no systemic effect at 10 ppm (equivalent to 0.5 mg/kg/day). The study was negative for carcinogenic effects under the conditions of the study at all feeding levels.
   - A 1-year and 180 day dog feeding studies with a NOEL for cholinesterase inhibition at 0.01 mg/kg/day and a LOEL of 0.03 mg/kg/day.
   - An 18-month mouse carcinogenicity study at dietary levels of 0, 2, 10, and 50 ppm (equivalent to 0.3, 1.5 and 7.5 mg/kg/day), which was negative for carcinogenic effects under the conditions of the study at all levels tested.

6. Carcinogenicity
   The HED Carcinogenicity Peer Review Committee has classified fenamiphos as a group E carcinogen (no evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiologic and animal studies) (EPA G. Ghali memo, 11/23/93). The same memo states that there was no evidence to suggest that the chemical was a developmental or reproductive toxicant.

7. Endocrine Effects
   No special studies investigating potential estrogenic or endocrine effects of fenamiphos have been conducted. However, the standard battery of required studies has been completed. These studies include an evaluation of the potential effects on reproduction and development and an evaluation of the pathology of the endocrine organs following repeated or long-term exposure. These studies are generally considered to be sufficient to detect any endocrine effects, but no such effects were noted in any of the studies with either fenamiphos or its metabolites.

8. Animal Metabolism
   A general rat metabolism study in which fenamiphos was metabolized to its sulfoxide and sulfone analogs with 50 percent excreted in the urine within 12 to 15 hours.

B. Aggregate Exposure

1. Dietary Exposure
   For purposes of assessing the potential acute and chronic dietary exposure, Bayer has estimated exposure using TAS Exposure Series, Version 4.12 computer software. This software uses the 1989-92 Nationwide Food Consumption Survey (NFCS) database to estimate acute and chronic exposures in the diet of the U.S. population and 22 population subgroups.

a. Acute

For acute dietary exposure the model calculates a margin of exposure (MOE) by dividing the estimated human exposure into the NOEL from the appropriate animal study. EPA has determined that endpoint for acute dietary assessment is 0.37 mg/kg/day based on the LOEL from a rat acute neurotoxicity study. In addition, the EPA has determined that an uncertainty factor of 300 should be used for enhanced sensitivity to infants and children. As a result, for acute dietary assessment, a margin of exposure (MOE) of 300 is required to ensure protection of infants and children.

The MOE for fenamiphos derived from previously established tolerances plus the proposed import tolerances on cantaloupe and coffee at the 99.9th percentile is 665 for the U.S. population and 357 for the most sensitive subpopulation (children, 1-6). These MOEs do not exceed the Agency's level of concern for acute dietary exposure.

b. Chronic

For purposes of assessing the potential chronic dietary exposure, the model uses the reference dose (RfD) which the EPA has determined to be 0.0001 mg/kg/day based on a NOEL of 0.01 mg/kg/day and an uncertainty factor of 100. The NOEL is based on results of a feeding study in beagle dogs which demonstrated plasma cholinesterase inhibition at the next highest dose. In addition, refinements in the residue values and percent crop treated information listed in EPA's October 28, 1994 memorandum (Dietary Risk Evaluation Section to the Reregistration Section), were used in calculating anticipated residues for registered uses. In order to assess the potential exposure from the proposed import tolerances on coffee and cantaloupe, Bayer has made the very conservative assumption that 100% of all cantaloupes (including those grown in the U.S.) and coffee will contain fenamiphos residues at the proposed tolerance level. This will result in a large overestimation of human exposure.

Using these conservative assumptions, the Anticipated Residue Contribution (ARC) for fenamiphos derived from previously established tolerances plus the proposed import tolerances on cantaloupe and coffee would be 0.000008 mg/kg bwt/day (7.6% of the RfD) for the U.S. population (48 states) and 0.000015 mg/kg bwt/day (14.8% of the RfD) for the most highly exposed population subgroup, children 1-6. Therefore, chronic dietary exposure from the existing and proposed uses will not exceed the reference dose for any subpopulation, including infants and children.

2. Drinking Water Exposure

The EFGWB had determined that fenamiphos has the potential to be highly mobile to mobile in the soil and its degradates appear to be more mobile than the parent fenamiphos. In field dissipation studies fenamiphos was not detected below 6 inches, and it had a half-life of 16.2 to 17 days. The degradates of fenamiphos were detected down to 36 inches in one of these studies.

Fenamiphos has been detected in groundwater as a result of a retrospective and a

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prospective groundwater monitoring study in Florida. These studies were conducted on citrus grown in sand. In addition, the EPA requested that Bayer conduct prospective groundwater studies in California on grapes and in Georgia on tobacco in order to better understand the fate of fenamiphos in the environment. These studies are currently underway. Fenamiphos or its degrades have not been detected in groundwater other than in the Florida citrus retrospective and prospective groundwater studies.

A lifetime Health Advisory Level (HAL) for fenamiphos has been established at 2 ppb. No HAL's have been established for the degradates of fenamiphos.

Since the proposed tolerances are for imported cantaloupe and coffee, there should be no exposure from fenamiphos in U.S. drinking water from these uses.

3. Non-occupational Exposure
Current Nemacur registrations are limited to commercial crop production, commercial ornamental (flowers and nursery stock) production and for use on turf (golf courses, cemeteries, sod farms and industrial grounds only). There are no residential turf or ornamental uses allowed. Therefore, there should be little if any exposure to infants and children from non-occupational exposure.

C. Cumulative Effects
Fenamiphos is an organophosphate nematicide/insecticide. Therefore, it has the same mechanism of activity as other organophosphate insecticides. At this time, the EPA has not made a determination of how cumulative risk assessments with other substances that may have a common mechanism of toxicity should be conducted. Therefore, for this tolerance petition, only the potential risks of fenamiphos are considered in its aggregate exposure.

D. Safety Determination
1. US General Population
a. Acute
As stated under Aggregate Exposure, the EPA has recommended that the LOEL from the rat acute neurotoxicity study (0.37 mg/kg/day) be used for acute dietary risk calculations. Based on the NFCS 1989-92 database, the margin of exposure (MOE) is 665 at the 99.9th percentile for the U.S. population. This MOE does not exceed the Agency's level of concern for acute dietary exposure.

b. Chronic
Using the conservative exposure assumptions described above under aggregate exposure and based on the completeness and reliability of the toxicity data, aggregate dietary exposure to fenamiphos from the previously established tolerances plus the pending import tolerances on cantaloupe and coffee will utilize 7.6% of the RfD for the U.S. population (48 states) and 14.8% of the RfD for the most highly exposed population subgroup, children, 1-6 years old. There is generally no concern for exposures below 100 percent of the RfD.

2. Infants and Children

a. Acute

As stated under Aggregate Exposure, the EPA has recommended that the LOEL from the rat acute neurotoxicity study (0.37 mg/kg/day) be used for acute dietary risk calculations. Based on the NFCS 1989-92 database, the MOE for the most sensitive population subgroup (children 1-6 years) is 357 at the 99.9th percentile. MOEs for the other population subgroups of concern are as follows: 665 for non-nursing infants, 636 for children 7-12 years, 1,347 for males 13-19 years, and 1,436 for females 13-19 years. These MOEs do not exceed the Agency's level of concern for acute dietary exposure.

b. Chronic

In assessing the potential for additional sensitivity of infants and children to residues of fenamiphos, the data from developmental studies in both rat and rabbit and a three-generation reproduction study in the rat should be considered. The developmental toxicity studies evaluate any potential adverse effects on the developing animal resulting from pesticide exposure of the mother during prenatal development. The reproduction study evaluates any effects from exposure to the pesticide on the reproductive capability of mating animals through several generations, as well as any observed systemic toxicity.

The rat developmental toxicity study shows a maternal NOEL of 0.85 mg/kg and a developmental NOEL of 3.0 mg/kg (HDT). The rabbit developmental toxicity study had both developmental and maternal NOELs at 0.5 mg/kg. The rat three-generation reproduction study showed no reproduction effects at 30 ppm. In all cases, the reproductive and developmental NOELs were greater than or equal to the parental NOELs. This indicates that fenamiphos does not pose any increased risk to infants or children. In addition, the EPA has stated that there is no evidence to suggest that fenamiphos is a developmental or reproductive toxicant (EPA G. Ghali memo, dated November 23, 1993).

FFDCA Section 408 provides that EPA may apply an additional safety factor for infants and children in the case of threshold effects to account for pre- and post-natal effects and the completeness of the toxicity database. Based on current toxicological data requirements, the EPA stated that the toxicology database for fenamiphos is complete and will support reregistration eligibility (EPA Esther Saito, Reregistration Branch letter, dated February 13, 1995). Further for fenamiphos, the NOEL of 0.01 mg/kg/bwt from the dog feeding study, which was used to calculate the RfD, is already lower than the NOELs from the developmental studies in rats (3 mg/kg bw/day) and rabbits (0.5 mg/kg bw/day). Since a 100-fold uncertainty factor is already used to calculate the RfD, an additional uncertainty factor is not warranted and the RfD at 0.0001 mg/kg/bwt/day is appropriate for assessing aggregate risk to infants and children.

Using the conservative exposure assumptions described above under aggregate exposure, Bayer has determined from a chronic dietary analysis that the percent of the RfD utilized by aggregate exposure to residues of fenamiphos ranges from 6.2% for children 7-12 years up to 14.8% for children 1-6 years.

EPA generally has no concern for exposure below 100 percent of the RfD. Therefore, based on the completeness and reliability of the toxicity data and the conservative exposure assessment, there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the residues of fenamiphos, including all anticipated dietary exposure and non-occupational exposures.

E. Residue Chemistry Data Summary

1. Residues in the Raw Agricultural Commodity and Processed Food/Feed

Cantaloupe

Four residue crop field trials were conducted in representative areas in Vera Cruz, Mexico. Nemacur 15% Granular was applied at planting in-furrow at the rate of 3 kg ai/hectare. Residues of fenamiphos in all samples were quantitated by gas chromatography. The limit of determination is 0.01 ppm. All residues in the pulp and whole fruit were <0.01 ppm.

Coffee

Four residue crop field trials were conducted in representative areas in Vera Cruz, Mexico. Each coffee bean tree received a pre-bloom in-furrow at the drip line application of Nemacur 15% Granular at the rate of 1.5 g ai/meter of tree height. Residues of fenamiphos in all samples were quantitated by gas chromatography. The limit of determination is 0.01 ppm. Residues in green coffee beans ranged from <0.01 to 0.1 ppm.

2. International Tolerances (Codex MRLs)

Codex MRLs have been established for residues of fenamiphos in melons at 0.05 ppm and in coffee beans at 0.1 ppm There are no established tolerances for fenamiphos in or on melons and coffee in Canada or Mexico.

3. Analytical Method

An enforcement method for plant commodities has been validated on various commodities. It has undergone successful EPA validation and has been submitted for inclusion in PAM II. The method should be adequate for imported cantaloupe and coffee beans. The animal method has also been approved as an adequate enforcement method.

4. Plant and livestock metabolism

The nature of the residue in plants and animals is adequately understood. The residue of concern is fenamiphos and its sulfone and sulfoxide metabolites as specified in 40 CFR 180.349, 185.2950 and 186.2950.

II. Background Information and Use Profile

A. Mode of Action

Fenamiphos, the active ingredient of Nemacur, is a contact organophosphate nematicide which also has activity against certain insect pests. It is systemic and is translocated both up and down within plants.

Fenamiphos is effective against all the major genera of plant parasitic nematodes,

particularly the widespread and highly damaging root-knot nematodes. Its mode of action is similar to that of other organophospates in that it inhibits cholinesterase activity in animals.

B. Use Pattern

Cantaloupe

The use pattern for the proposed import tolerance in/on cantaloupe calls for the use of 30 kilograms of Nemacur 10% Granular (3 kg active) per hectare incorporated into the seed furrow at planting. Only one application is permitted per season. The PHI is 60 days.

Coffee

The use pattern for the proposed import tolerance in/on coffee calls for the use of 15 grams of Nemacur 10% Granular (1.5 grams active) per meter of tree height applied in-furrow at the drip line at the pre-bloom stage. Only one application is permitted per season. The PHI is 150 days.

III. Risk Assessment and Statutory Findings

A. Toxicological Profile

1. Acute Toxicity
   - Rat acute oral study with an LD50 of 2.7 mg/kg for males and 3.0 mg/kg for females
   - Rabbit acute dermal of LD50 of 225 mg/kg for males and 178.8 mg/kg for females
   - Rat acute inhalation of LC50 of > 0.1 mg/L
   - Primary eye irritation study in the rabbit which showed slight irritation
   - Primary dermal irritation study showed no skin irritation
   - Primary dermal sensitization study showed no sensitization
   - Acute delayed neurotoxicity study showed that fenamiphos is not neurotoxic
   - Acute oral neurotoxicity study showed no treatment-related changes in mean body weights, absolute and relative brain weights and the incidence of gross and neurohistopathological lesions. Clinical signs were observed including plasma and red blood cell inhibition. The LOEL is 0.37 mg/kg. The NOEL was not identified.

2. Genotoxicity
   - An Ames study was negative.
   - A dominant-lethal test in mice was negative.
   - An in vitro assay in Chinese hamster ovary cells was negative.

3. Reproductive and Developmental Toxicity
   - A three-generation reproduction study with no reproductive effects at 30 ppm (HDT).
   - A teratology study in rabbits with developmental and maternal NOELs at 0.5 mg/kg.
   - A teratology study in rats with a maternal NOEL of 0.85 mg/kg and a developmental NOEL of 3.0 mg/kg (HDT).

4. Subchronic Toxicity
   - A 90-day rat feeding study with a no-observed-effect level (NOEL) of 4 ppm for cholinesterase inhibition.
   - A 90-day dog-feeding study with a NOEL of 1 ppm for cholinesterase inhibition.
   - A 21-day dermal exposure study showing no effects on plasma, erythrocyte, or brain cholinesterase activity at 0.5 mg/kg.
   - A 21-day inhalation study with a cholinesterase NOEL of 0.25 μg/L and a LEL of 3.5 μg/L.
   - A neurotoxicity study in hens showed no neurotoxicity damage at 12.5 mg/kg (HDT).
   - A subchronic neurotoxicity screen study showed no treatment-related changes in mean body weights or absolute and relative brain weights. The incidences of gross and neuropathological findings of treated animals were comparable to controls. Based on plasma and red blood cell inhibition the LOEL was established at 10 ppm and the NOEL at 1 ppm.
5. Chronic Toxicity
   - A 2-year rat feeding/carcinogenicity study with a NOEL for cholinesterase inhibition at less than 2.0 ppm (equivalent to 0.1 mg/kg/day) and no systemic effect at 10 ppm (equivalent to 0.5 mg/kg/day). The study was negative for carcinogenic effects under the conditions of the study at all feeding levels.
   - A 1-year and 180 day dog feeding studies with a NOEL for cholinesterase inhibition at 0.01 mg/kg/day and a LOEL of 0.03 mg/kg/day.
   - An 18-month mouse carcinogenicity study at dietary levels of 0, 2, 10, and 50 ppm (equivalent to 0.3, 1.5 and 7.5 mg/kg/day), which was negative for carcinogenic effects under the conditions of the study at all levels tested.

6. Carcinogenicity
   The HED Carcinogenicity Peer Review Committee has classified fenamiphos as a group E carcinogen (no evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiologic and animal studies) (EPA G. Ghali memo, 11/23/93). The same memo states that there was no evidence to suggest that the chemical was a developmental or reproductive toxicant.

7. Endocrine Effects
   No special studies investigating potential estrogenic or endocrine effects of fenamiphos have been conducted. However, the standard battery of required studies has been completed. These studies include an evaluation of the potential effects on reproduction and development and an evaluation of the pathology of the endocrine organs following repeated or long-term exposure. These studies are generally considered to be sufficient to detect any endocrine effects, but no such effects were noted in any of the studies with either fenamiphos or its metabolites.

8. Animal Metabolism
   A general rat metabolism study in which fenamiphos was metabolized to its sulfoxide and sulfone analogs with 50 percent excreted in the urine within 12 to 15 hours.

B. Aggregate Exposure

1. Dietary Exposure

For purposes of assessing the potential acute and chronic dietary exposure, Bayer has estimated exposure using TAS Exposure Series, Version 4.12 computer software. This software uses the 1989-92 Nationwide Food Consumption Survey (NFCS) database to estimate acute and chronic exposures in the diet of the U.S. population and 22 population subgroups.

a. Acute

For acute dietary exposure the model calculates a margin of exposure (MOE) by dividing the estimated human exposure into the NOEL from the appropriate animal study. EPA has determined in its Science Analysis Branch, Health Effects Division's September 18, 1997 memorandum that endpoint for acute dietary assessment is 0.37 mg/kg/day based on the LOEL from a rat acute neurotoxicity study. In addition, the EPA has determined that an uncertainty factor of 300 should be used for enhanced sensitivity to infants and children since a NOEL was not established in the rat acute neurotoxicity study. As a result, for acute dietary assessment, a margin of exposure (MOE) of 300 is now required to ensure protection of infants and children.

The MOE for fenamiphos derived from previously established tolerances plus the proposed import tolerances on cantaloupe and coffee at the 99.9th percentile is 665 for the U.S. population and 357 for the most sensitive subpopulation (children, 1-6) (Attachment A). These MOEs do not exceed the Agency's level of concern for acute dietary exposure.

b. Chronic

For purposes of assessing the potential chronic dietary exposure, the model uses the reference dose (RfD) which the EPA has determined to be 0.0001 mg/kg/day based on a NOEL of 0.01 mg/kg/day and an uncertainty factor of 100. The NOEL is based on results of a feeding study in beagle dogs which demonstrated plasma cholinesterase inhibition at the next highest dose. In addition, refinements in the residue values and percent crop treated information listed in EPA's October 28, 1994 memorandum (Dietary Risk Evaluation Section to the Reregistration Section), were used in calculating anticipated residues for registered uses. In order to assess the potential exposure from the proposed import tolerances on coffee and cantaloupe, Bayer has made the very conservative assumption that 100% of all cantaloupes (including those grown in the U.S.) and coffee will contain fenamiphos residues at the proposed tolerance level. This will result in a large overestimation of human exposure.

Using these conservative assumptions, the Anticipated Residue Contribution (ARC) for fenamiphos derived from previously established tolerances plus the proposed import tolerances on cantaloupe and coffee would be 0.000008 mg/kg bwt/day (7.6% of the RfD) for the U.S. population (48 states) and 0.000015 mg/kg bwt/day (14.8% of the RfD) for the most highly exposed population subgroup, children 1-6. (Attachment B). Therefore, chronic dietary exposure from the existing and proposed uses will not exceed the reference dose for any

subpopulation, including infants and children.

2. Drinking Water Exposure
The EFGWB had determined that fenamiphos has the potential to be highly mobile to mobile in the soil and its degradates appear to be more mobile than the parent fenamiphos. In field dissipation studies fenamiphos was not detected below 6 inches, and it had a half-life of 16.2 to 17 days. The degradates of fenamiphos were detected down to 36 inches in one of these studies.

Fenamiphos has been detected in groundwater as a result of a retrospective and a prospective groundwater monitoring study in Florida. These studies were conducted on citrus grown in sand. In addition, the EPA requested that Bayer conduct prospective groundwater studies in California on grapes and in Georgia on tobacco in order to better understand the fate of fenamiphos in the environment. These studies are currently underway. Fenamiphos or its degrades have not been detected in groundwater other than in the Florida citrus retrospective and prospective groundwater studies.

A lifetime Health Advisory Level (HAL) for fenamiphos has been established at 2 ppb. No HAL's have been established for the degradates of fenamiphos.

Since the proposed tolerances are for imported cantaloupe and coffee, there should be no exposure from fenamiphos in U.S. drinking water from these uses.

3. Non-occupational Exposure
Current Nemacur registrations are limited to commercial crop production, commercial ornamental (flowers and nursery stock) production and for use on turf (golf courses, cemeteries, sod farms and industrial grounds only). There are no residential turf or ornamental uses allowed. Therefore, there should be little if any exposure to infants and children from non-occupational exposure.

C. Cumulative Effects
Fenamiphos is an organophosphate nematicide/insecticide. Therefore, it has the same mechanism of activity as other organophosphate insecticides. At this time, the EPA has not made a determination of how cumulative risk assessments with other substances that may have a common mechanism of toxicity should be conducted. Therefore, for this tolerance petition, only the potential risks of fenamiphos are considered in its aggregate exposure.

D. Safety Determination
1. US General Population
a. Acute
As stated under Aggregate Exposure, the EPA has recommended that the LOEL from the rat acute neurotoxicity study (0.37 mg/kg/day) be used for acute dietary risk calculations. Based on the NFCS 1989-92 database, the margin of exposure (MOE) is 665 at the 99.9th percentile for the U.S. population (Attachment A). This MOE does not exceed the Agency's level of concern for acute dietary exposure.

b. Chronic

Using the conservative exposure assumptions described above under aggregate exposure and based on the completeness and reliability of the toxicity data, aggregate dietary exposure to fenamiphos from the previously established tolerances plus the pending import tolerances on cantaloupe and coffee will utilize 7.6% of the RfD for the U.S. population (48 states) and 14.8% of the RfD for the most highly exposed population subgroup, children, 1-6 years old (Attachment B). There is generally no concern for exposures below 100 percent of the RfD.

2. Infants and Children

a. Acute

As stated under Aggregate Exposure, the EPA has recommended that the LOEL from the rat acute neurotoxicity study (0.37 mg/kg/day) be used for acute dietary risk calculations. Based on the NFCS 1989-92 database, the MOE for the most sensitive population subgroup (children 1-6 years) is 357 at the 99.9th percentile. MOEs for the other population subgroups of concern are as follows: 665 for non-nursing infants, 636 for children 7-12 years, 1,347 for males 13-19 years, and 1,436 for females 13-19 years (Attachment A). These MOEs do not exceed the Agency's level of concern for acute dietary exposure.

b. Chronic

In assessing the potential for additional sensitivity of infants and children to residues of fenamiphos, the data from developmental studies in both rat and rabbit and a three-generation reproduction study in the rat should be considered. The developmental toxicity studies evaluate any potential adverse effects on the developing animal resulting from pesticide exposure of the mother during prenatal development. The reproduction study evaluates any effects from exposure to the pesticide on the reproductive capability of mating animals through several generations, as well as any observed systemic toxicity.

The rat developmental toxicity study shows a maternal NOEL of 0.85 mg/kg and a developmental NOEL of 3.0 mg/kg (HDT). The rabbit developmental toxicity study had both developmental and maternal NOELs at 0.5 mg/kg. The rat three-generation reproduction study showed no reproduction effects at 30 ppm. In all cases, the reproductive and developmental NOELs were greater than or equal to the parental NOELs. This indicates that fenamiphos does not pose any increased risk to infants or children. In addition, the EPA has stated that there is no evidence to suggest that fenamiphos is a developmental or reproductive toxicant (EPA G. Ghali memo, dated November 23, 1993).

FFDCA Section 408 provides that EPA may apply an additional safety factor for infants and children in the case of threshold effects to account for pre- and post-natal effects and the completeness of the toxicity database. Based on current toxicological data requirements, the EPA stated that the toxicology database for fenamiphos is complete and will support reregistration eligibility (EPA Esther Saito, Reregistration Branch letter, dated February 13, 1995). Further for

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fenamiphos, the NOEL of 0.01 mg/kg/bwt from the dog feeding study, which was used to calculate the RfD, is already lower than the NOELs from the developmental studies in rats (3 mg/kg bw/day) and rabbits (0.5 mg/kg bw/day). Since a 100-fold uncertainty factor is already used to calculate the RfD, an additional uncertainty factor is not warranted and the RfD at 0.0001 mg/kg/bwt/day is appropriate for assessing aggregate risk to infants and children.

Using the conservative exposure assumptions described above under aggregate exposure, Bayer has determined from a chronic dietary analysis (Attachment B) that the percent of the RfD utilized by aggregate exposure to residues of fenamiphos ranges from 6.2% for children 7-12 years up to 14.8% for children 1-6 years. EPA generally has no concern for exposure below 100 percent of the RfD. Therefore, based on the completeness and reliability of the toxicity data and the conservative exposure assessment, there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the residues of fenamiphos, including all anticipated dietary exposure and non-occupational exposures.

IV. Residue Chemistry Data Summary

A. Residues in the Raw Agricultural Commodity and Processed Food/Feed

Cantaloupe

Four residue crop field trials were conducted in representative areas in Vera Cruz, Mexico. Nemacur 15% Granular was applied at planting in-furrow at the rate of 3 kg ai/hectare. Residues of fenamiphos in all samples were quantitated by gas chromatography. The limit of determination is 0.01 ppm. All residues in the pulp and whole fruit were <0.01 ppm.

Coffee

Four residue crop field trials were conducted in representative areas in Vera Cruz, Mexico. Each coffee bean tree received a pre-bloom in-furrow at the drip line application of Nemacur 15% Granular at the rate of 1.5 g ai/meter of tree height. Residues of fenamiphos in all samples were quantitated by gas chromatography. The limit of determination is 0.01 ppm. Residues in green coffee beans ranged from <0.01 to 0.1 ppm.

B. International Tolerances (Codex MRLs)

Codex MRLs have been established for residues of fenamiphos in melons at 0.05 ppm and in coffee beans at 0.1 ppm There are no established tolerances for fenamiphos in or on melons and coffee in Canada or Mexico.

C. Analytical Method

An enforcement method for plant commodities has been validated on various commodities. It has undergone successful EPA validation and has been submitted for inclusion in PAM II. The method should be adequate for imported cantaloupe and coffee beans. The animal method has also been approved as an adequate enforcement method.

D. Plant and livestock metabolism
The nature of the residue in plants and animals is adequately understood. The residue of concern is fenamiphos and its sulfone and sulfoxide metabolites as specified in 40 CFR 180.349, 185.2950 and 186.2950.

E. Pending Tolerances and Exemptions
Petitions are currently pending with the Agency to establish tolerances permitting use of fenamiphos on almonds and pecans (PP: 5F4556); broccoli and cauliflower (PP: 0F3894); Melons/cucurbits (IR-4 Petition) (PP: 5E3178); peanuts (PP: 7F3523); bell and non-bell peppers (IR-4 Petition) (PP: 2E4047); plums, prunes and walnuts (0F3915); and potatoes (PP: 6F1693).